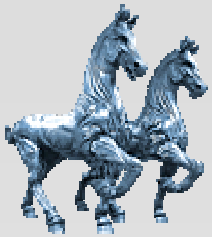

Biological Warfare Defense at DARPA
Program Overview

Stephen S. Morse, Ph.D.
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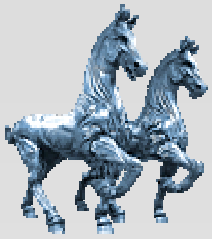
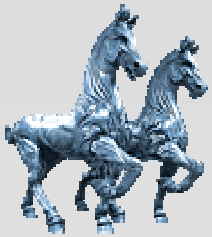


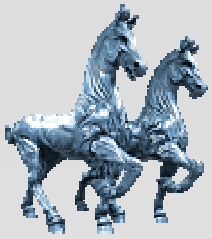
DARPA BWD Program

Goal: Develop and demonstrate technologies to thwart the use of biological warfare agents (including novel or bioengineered pathogens) **by both military and terrorist opponents.**



DARPA BWD Program

Approach: **Create technologies applicable to broad classes of pathogens and toxins** (most current techniques are agent specific).



DARPA BWD Program

Measures of Success:

- *in vivo* testing (vs. *in vitro*)
- live agent (vs. inactivated)
- significant pathogen/toxins (vs. simulants)
- integration and utilization

BWD Program Overview

Minutes to Hours

Minutes to Hours

Hours to Days

Hours to Days

Bio Event

Sensors

External Protection

Consequence Management

- Advanced Diagnostics
- Medical Countermeasures

Genomic Sequencing

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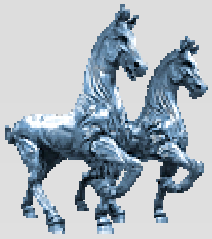


DARPA BWD Program

Sensors
Dr. Mildred Donlon
Dr. Alan S. Rudolph
Dr. John K. Smith

Advanced Diagnostics
Dr. Stephen Morse

Medical Countermeasures
CDR Shaun B. Jones, M.D., USN

External Protection
Dr. William Warren
CDR Shaun B. Jones M.D., USN

Genomic Sequencing
Dr. Ira Skurnick

Consequence Management
Col John Silva, M.D., USAF

DSO

BWD Program Overview

Bio Event

External Protection

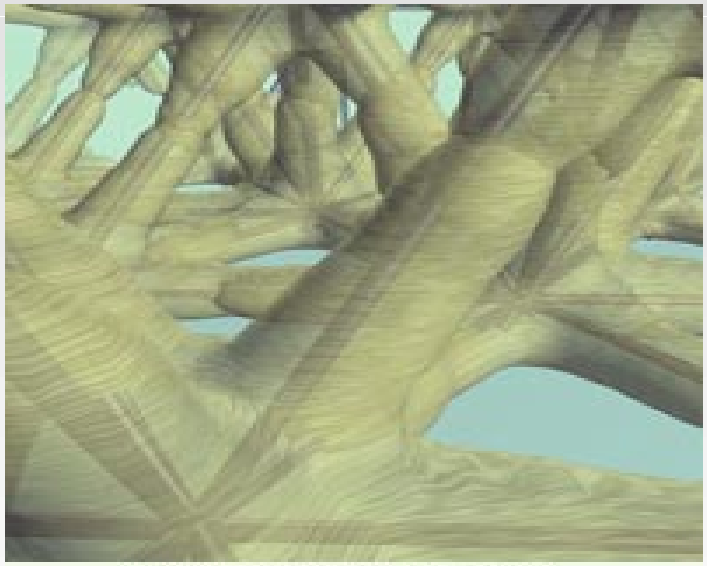
DSO

External Protection

Thermo-Catalytic Approach to "Clean Air"

- Pass hot air thru catalytic reactor to destroy lethal agents
- Heat & cool air in meso-heat exchangers
- Small, lightweight

"Artificial Skins"

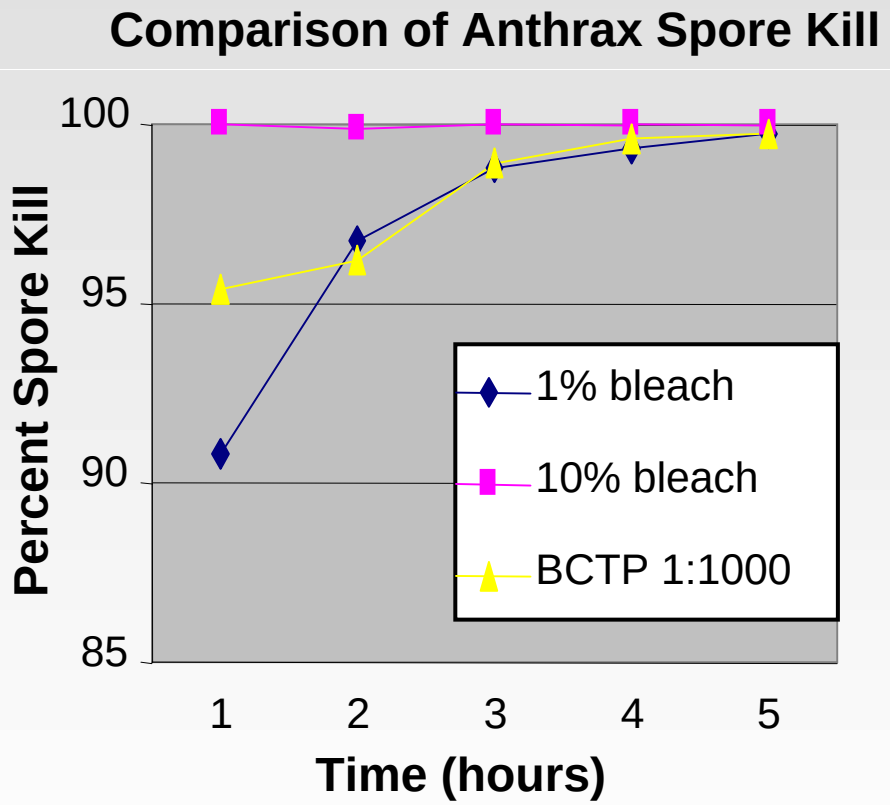


Coat polymer scaffolds with high surface area aerogels incorporating enzymes to promote biocatalysis

DSO

Nanomolecular Countermeasures

- Novasomes™ have significant bactericidal effect (> 99% killed) on gram positive bacteria and spores
- Novasomes™ can be used to decontaminate vehicles and sensitive equipment
- Novasomes™ are non-toxic to humans, plants, and animals



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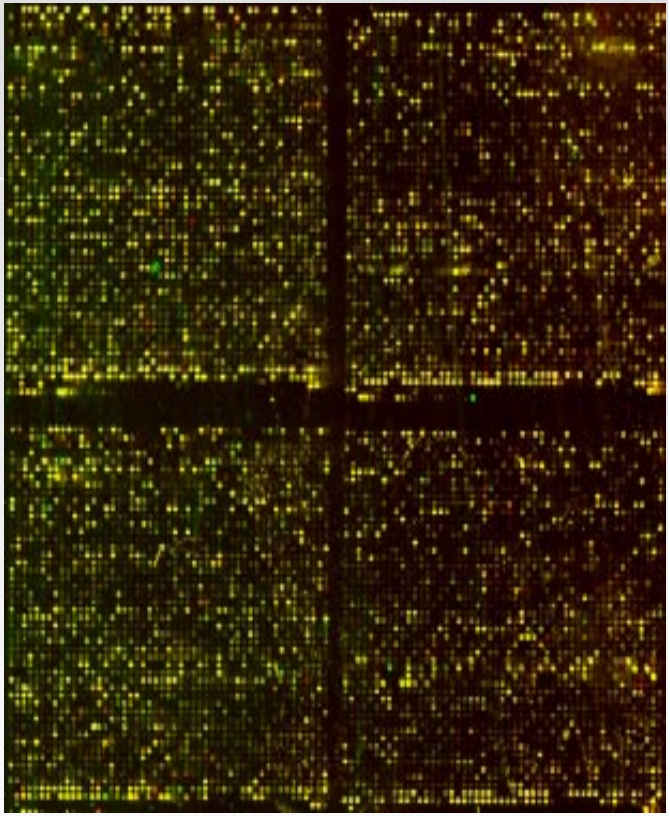
BWD Program Overview

Bio Event

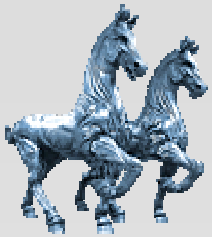
Advanced Diagnostics

Advanced Diagnostics for BWD



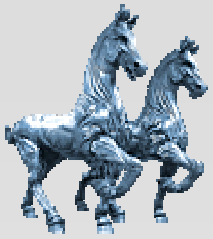
Goals:

- Detect exposure/infection by any biological threat agent, and differentiate from other significant pathogens
  - – in the body/clinical samples
  - – in real-time
  - – before symptoms appear
- Monitor the effectiveness of therapy



The Need for Advanced Diagnostics

- During conflicts, 75% of casualties are disease non-battle injury
- Infections by different biological warfare agents may begin with the same flu-like symptoms, but have very different outcomes
- Effective treatment requires correct early diagnosis and pathogen identification



Advanced Diagnostics for BWD

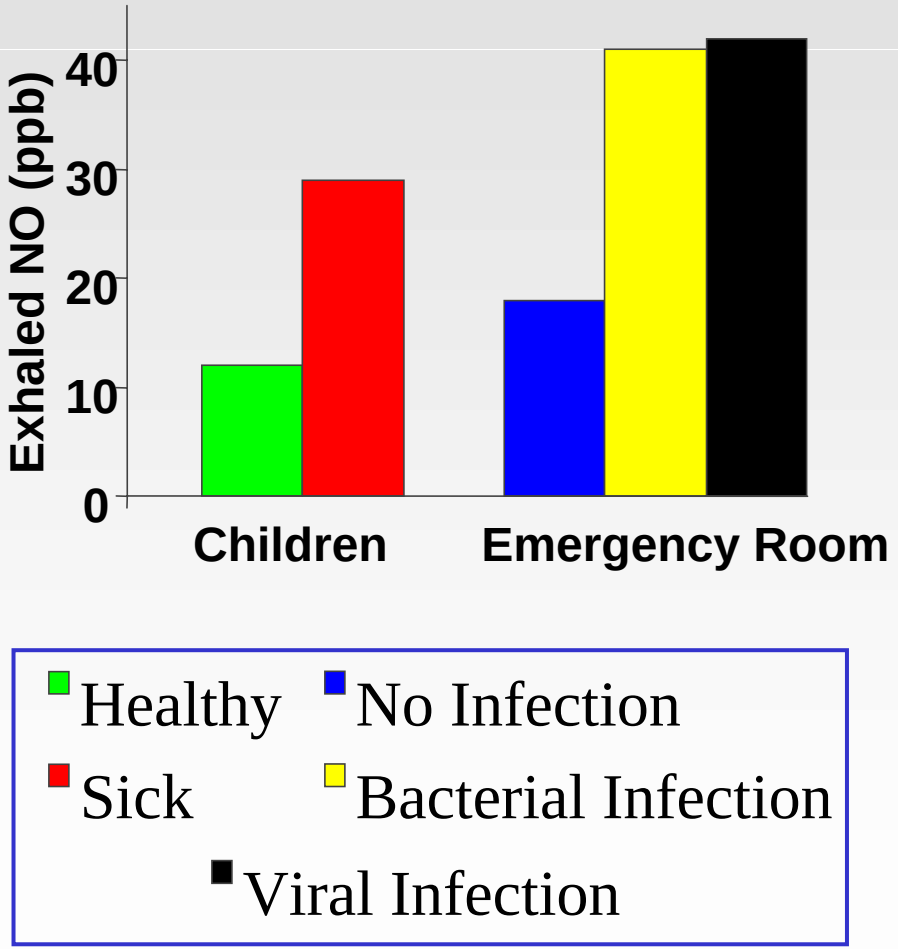
Approach:

- Leverage developments in commercial biotechnology (e.g., “PCR-on-a-chip”)
- Develop new diagnostic technologies (e.g., rapid agent identification, cellular sentries)
- Identify new markers of diseases and develop into new diagnostic capabilities (e.g., exhaled NO detection)

"BW Breathalyzer"

Summary of Clinical Studies

- Exhaled NO levels are greater in symptomatic subjects
- NO increases early in infection, sometimes *before* self-reported symptoms change
- Prototype NO sensors developed



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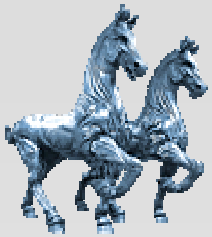
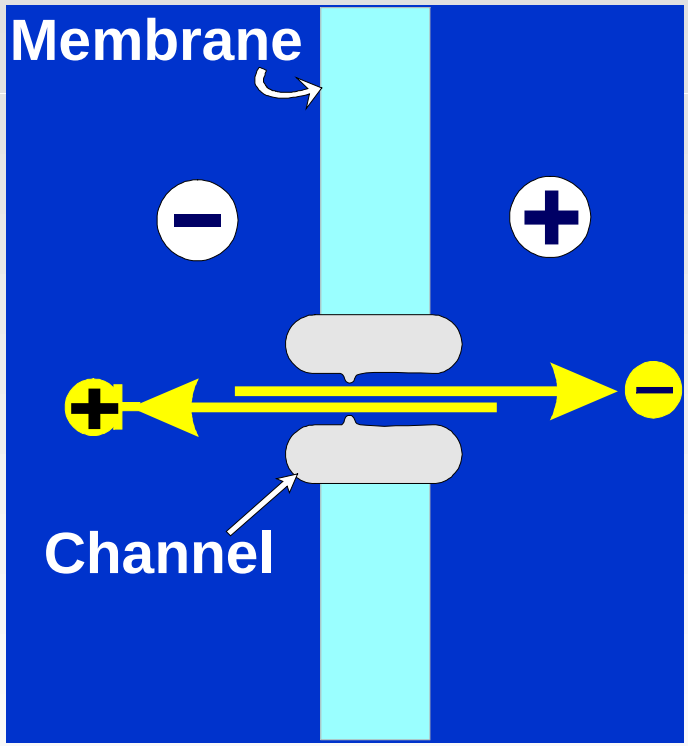
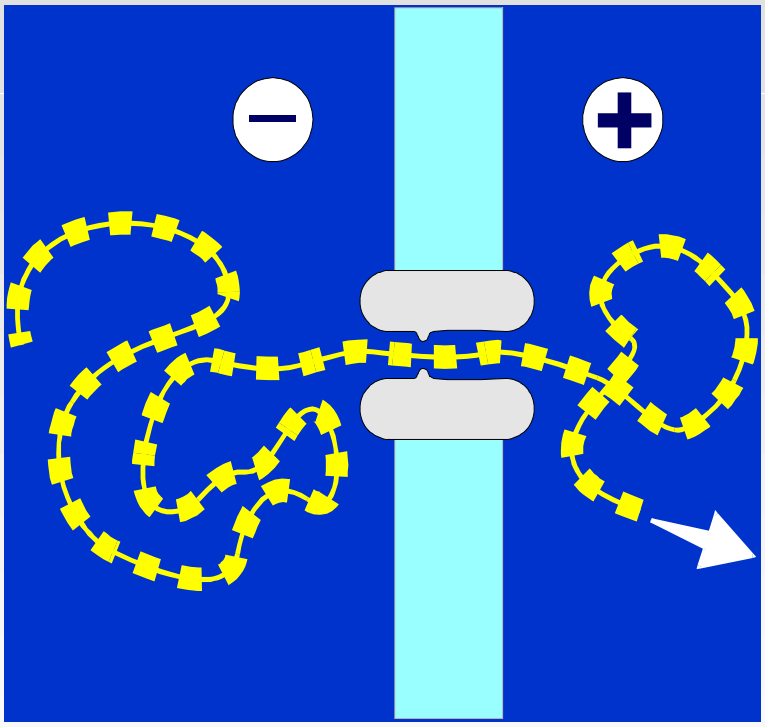


Single-Chain DNA Sequencing



Ions flow through an open channel

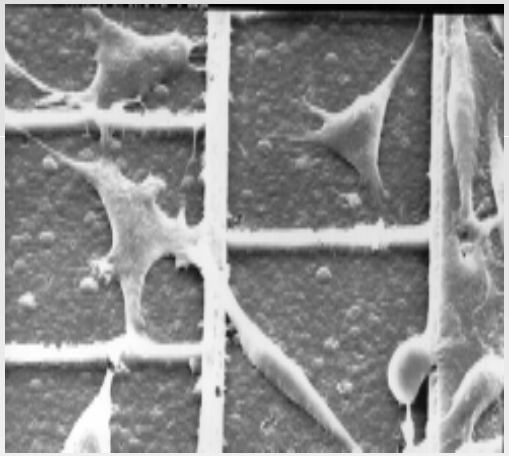


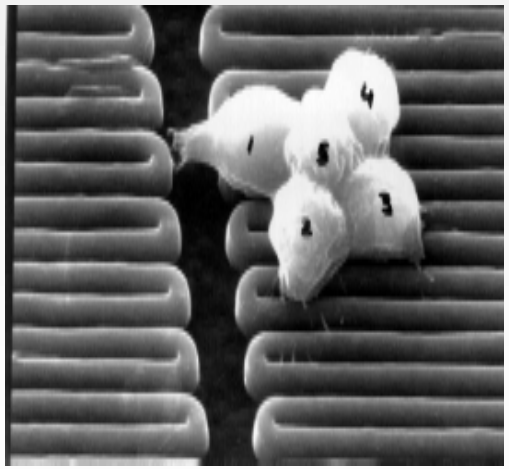
Reduction of ion flux reflects the properties of the nucleotide

Tissue Based Biosensors

Goal:

Develop multifunctional physiological bioassay system(s) utilizing singular and multicellular arrays to provide early warning for chem/bio agents (toxins, nerve agents, bioregulators and other chemicals)





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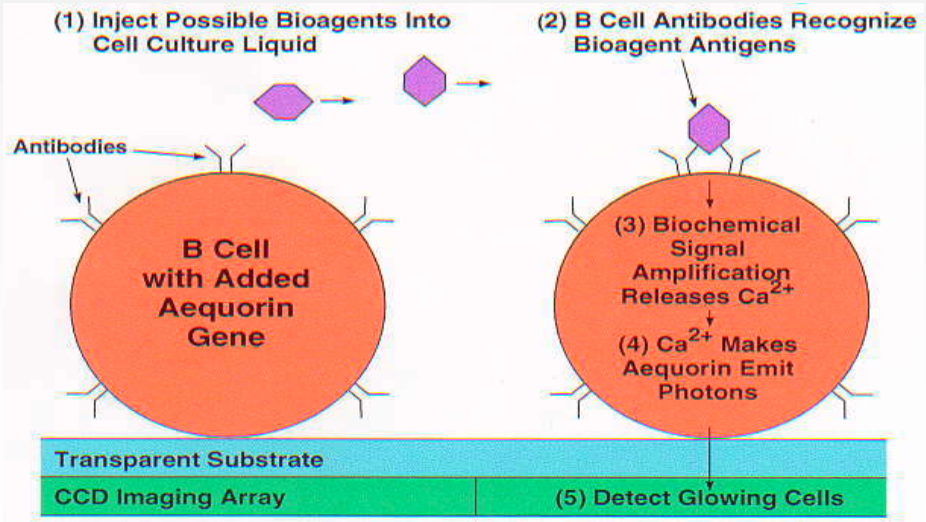
B-Cell Amplifier "CANARY"

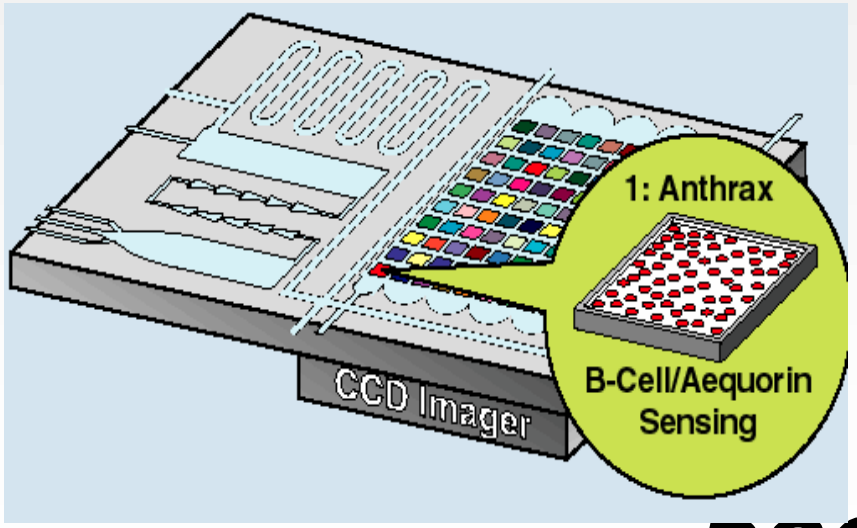
Objective:

Use genetically modified cells as amplifiers for single particle detection of pathogens

Approach:

Engineer B-cells with a bio-luminescent protein to signal binding; integrate into a microfluidic chip

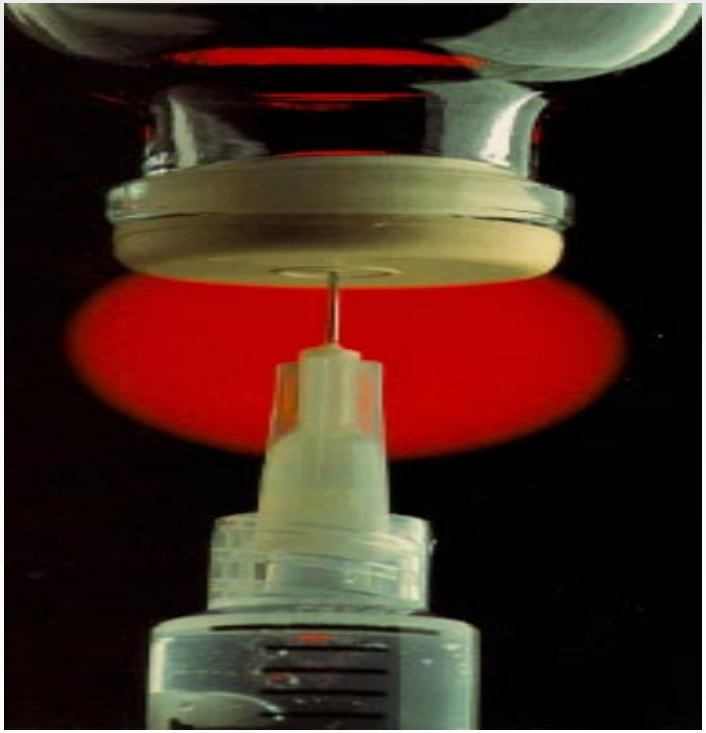




DSO

BWD Program Overview

Bio Event



Medical Countermeasures

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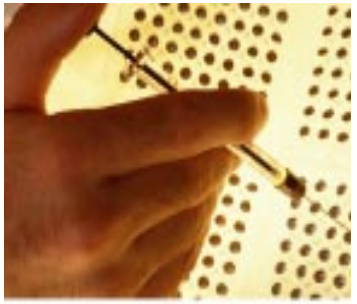
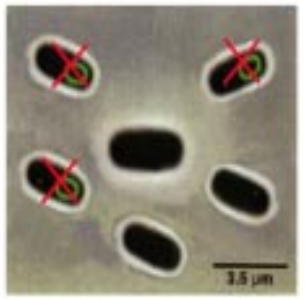
Medical Countermeasures

Program Goals:

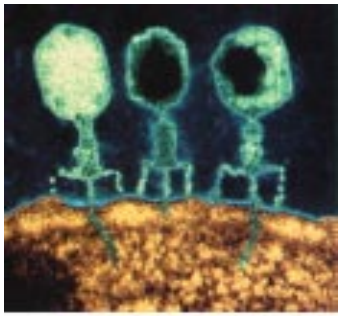
- Defeat a pathogen's ability to enter the body and reach target tissues
- Target common mechanisms of pathogenesis and functions or structures shared by groups of pathogens
- Modulate the human biological response to pathogens



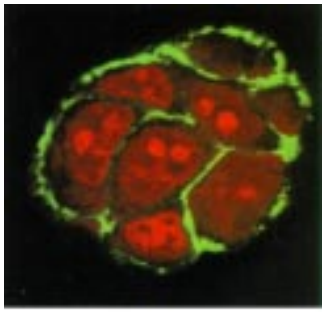
Rapid Immunizations



Anti-Bacterials



Anti-Virals



Anti-Toxins

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Revolutionary Approaches to Vaccines

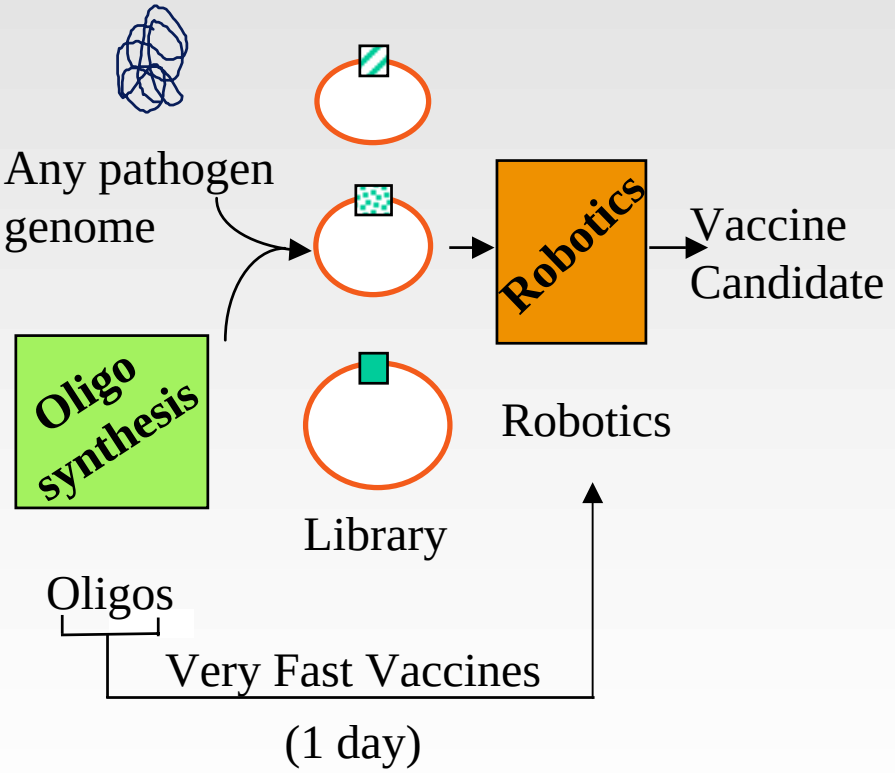
Fast acting
potent vaccines

Inducible
vaccine boosts

Systematic
vaccine production

Vaccines
in a day

High Throughput Vaccine Production



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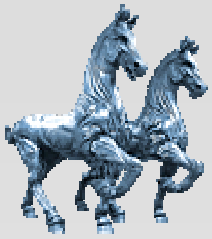
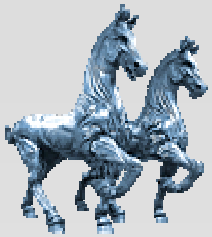


Early Pathogen Genes

Why target genes turned on early?

- Likely to be important for the pathogen to establish infection
- Many of the most "generic" virulence steps (e.g., pathogen-host signaling mechanisms) are expressed early → identification of broadly applicable targets
- Want to treat patient as early as possible to minimize illness or death



Early Pathogen Genes

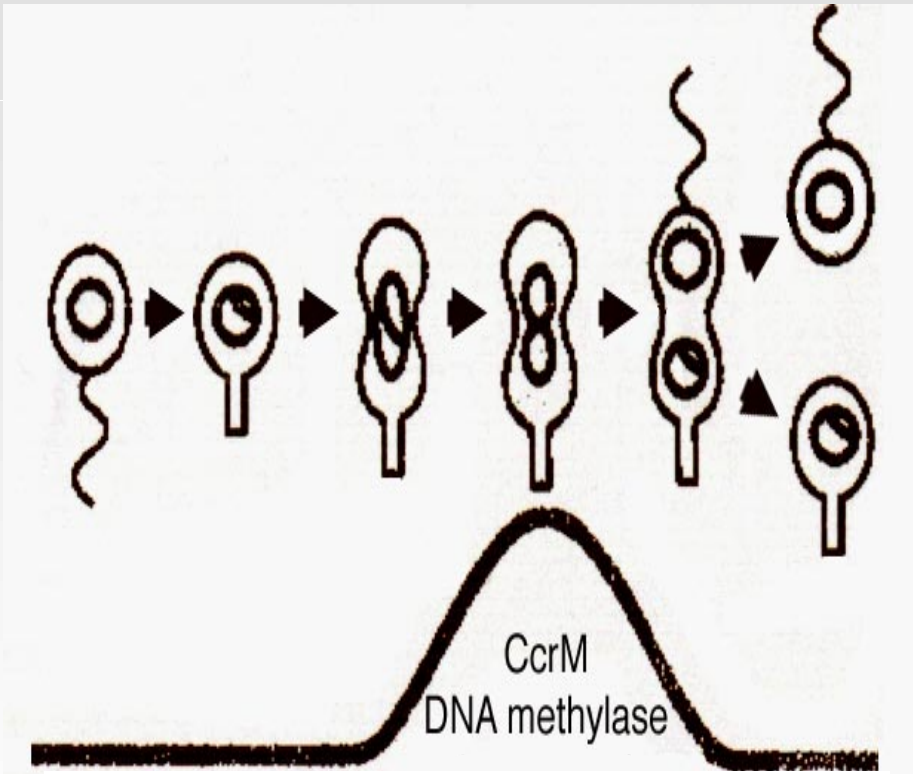
Results:

- Identified over 200 genes **that are turned on early in the infection process and are shared by multiple pathogens**
- Identified 22 Two-Component Signal Transduction systems, critical to the pathogen because they sense the environment and ensure microbial adaptation
- Identifying and developing candidate therapeutics based on these functions

Enzymes Essential for Pathogen Survival

Target a newly discovered enzyme (CcrM) essential to bacterial pathogen survival

- First target Brucella abortus
- Identical target found in many other plant and animal pathogens
- Candidate compounds now being tested

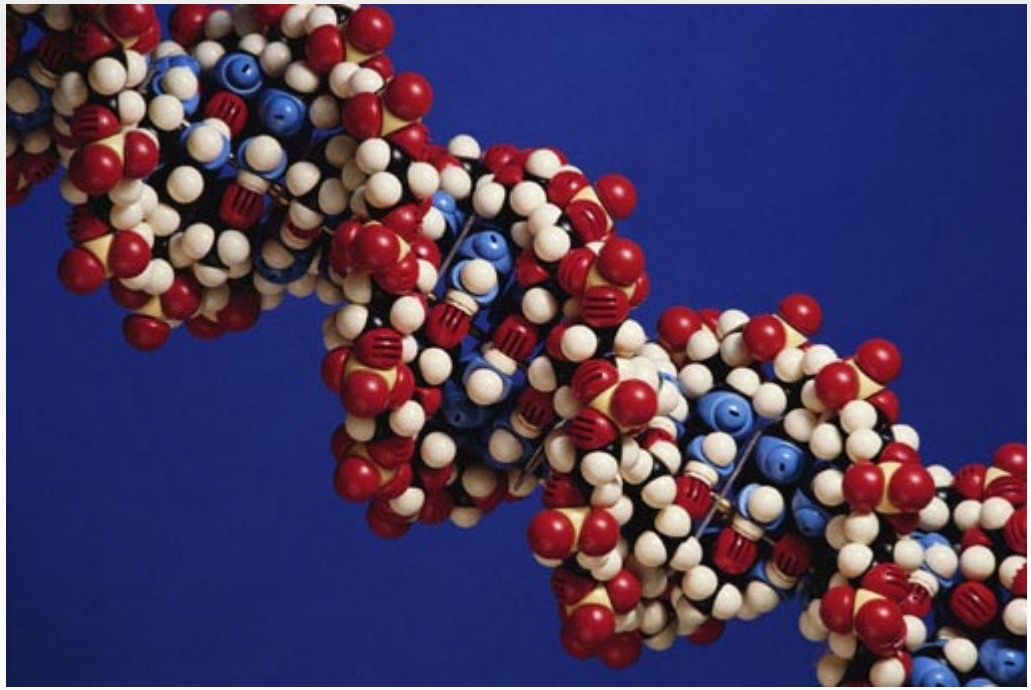


Level and Timing of CcrM in Cell Cycle Critical to Bacterial Viability

DSO

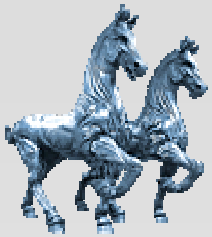
BWD Program Overview

Bio Event



Genomic Sequencing

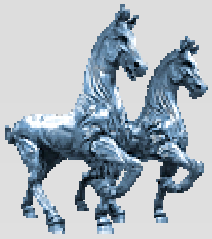
DSO



BWD Genomic Sequencing

Goals:

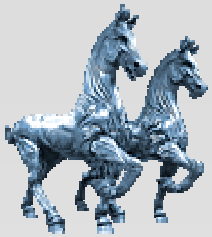
- Develop inventory of genes and proteins that distinguish pathogens from non-pathogens … look for general rules or patterns
- Identify pathogenic markers in any guise
- Provide superior molecular targets for identification and treatment



BWD Genomic Sequencing

Approach:

- Sequence/annotate biological threat agents (viruses, bacteria and rickettsia) and their respective non-pathogenic “nearest neighbors”
- Identify genes and proteins whose expression is essential for pathogenesis
- Identify coordinately regulated genes/proteins and common regulatory elements



BWD Website

http://www.darpa.mil/DSO/rd/Abmt/Bwd.html